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TITLE : AGENT FOR PROMOTING SYNTHESIS OF COLLAGEN

ABSTRACT : PROBLEM TO BE SOLVED: To prepare an agent for promoting the synthesis of collagen, having collagen synthesis-accelerating effect excellent in stability and capable of providing cosmetics excellent in wrinkle-improving effect by including a specific ascorbic acid (derivative), a nonionic surfactant and neutral fat.

SOLUTION: This agent for promoting the synthesis of collagen is prepared by including (A) 1-70 wt.% L-ascorbic acid or its derivative (e.g. L-ascorbyl-2- phosphate) each in a state of ultra fine particles having ≤3 μm (preferably ≤1 μm, more preferably ≤0.5 μm) average particle diameter preferably subjected to physical crushing, (B) a nonionic surfactant (e.g. polyglycerin-condensed ricinolein) preferably having ≤4 HLB in a 1-100 wt.% bases on the quantity of the ingredient C and (C) a neutral fat (e.g. a triglyceride of a fatty acid having a medium-sized chain) preferably having ≤45°C melting point (more preferably having a melting point lower than room temperature) in a W/O form where the ingredient A is dispersed in the ingredients B and C.

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## CLAIMS

[Claim(s)]
[Claim 1]A collagen synthesis accelerator containing at least one sort and a nonionic surface active agent which are chosen from a group which consists of L-ascorbic acid and its derivative, and neutral lipid.
[Claim 2]The collagen synthesis accelerator according to claim 1, wherein at least one sort chosen from a group which consists of L-ascorbic acid and its derivative is a solid not more than mean-particle-diameter 3micrometer.
[Claim 3]The collagen synthesis accelerator according to claim 1 or 2, wherein a nonionic surface active agent is four or less HLB.
[Claim 4]claims 1-3, wherein the melting point of neutral lipid is 45 ** or less -- a collagen synthesis accelerator given in any or the 1st paragraph.
[Claim 5]claims 1-4 -- a skin cosmetic containing a collagen synthesis accelerator of a statement in any or the 1st paragraph.

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## DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention]A skin cosmetic, wherein this invention contains the collagen synthesis accelerator and it which contain at least one sort (it is called L-ascorbic acid below) chosen from the group which consists of L-ascorbic acid and its derivative as physiologically active components (a quasi-drugs slack medicated cosmetic is included.) It is below the same. It is related.
[0002]
[Description of the Prior Art]The fortification of drugs, cosmetics, and foodstuffs or a use extensive as an antioxidant is presented with L-ascorbic acid by the unique physiological function. The melanin generation depressor effect of the epidermis melanocyte which L-ascorbic acid has especially, and the inflammation depressor effect by ultraviolet rays, The collagen formation facilitatory effect of cutis fibroblast is used, and it is used widely by aging prevention cosmetics aiming at prevention, whitening cosmetics aiming at a therapy and prevention of wrinkles, and skin moisturization of the stain of skin, a freckle, etc. However, L-ascorbic acid has the fault of being unstable, to oxidation, heat, and light so that it may be represented by L-ascorbic acid.
[0003]How to replace some functional groups of L-ascorbic acid molecules, such as esterification (JP,55-45546,B etc.) and phosphorylation with fatty acid, and complex-salt-izing (JP,7-53581,A etc.), by a suitable substituent as a stabilization process of L-ascorbic acid, Or the method (JP,57-48050,B) of using amino acid and organic acid together as a stabilizing agent, etc. are proposed. However, since the preservation stability of above-mentioned L-ascorbic acid and its derivative could not yet be insufficient or heat sterilization etc. were not able to be borne, when it applied to the skin, sufficient effect was not acquired, and a collagen synthesis facilitatory effect was not fully accepted in many cases. These derivatives cause the

fall of the medicinal value of L-ascorbic acid, and they have problems, such as a manifestation of side effects.

[0004]When using amino acid and organic acid together as a stabilizing agent, it is generated by ammonia etc. according to the oxidation state and pH condition of L-ascorbic acid itself, and there are problems, such as having on use the influence which is not preferred in a smell.

[0005]The solution of the method (JP,57-48050,B) of mixing and covering L-ascorbic acid and its salts simple substance into the mixture of fats and oils with a melting point of 50-80 ** and an emulsifier, L-ascorbic acid, and its salts In addition, an oleophilic sorbitan fatty acid ester, The methods (JP,63-96727,B, JP,6-343400,A, etc.) of making emulsify in the fats and oils which added sucrose fatty acid ester, polyglycerin condensation ricinoleic acid ester, etc., and using as a water-in-oil type (W/O) emulsifying-oil fat constituent, etc. are proposed.

[0006]However, it is the method of the solid fats and oils of a high-melting point covering the crystal surface of L-ascorbic acid in the former, and making the solid / solid interface of W/O distributed type forming, Although excelled in the stability of L-ascorbic acid, the L-ascorbic acid crystal to be used is a not less than tens of micrometers big and rough crystal, in order to succeed in the about 0.2-2-mm granular gestalt covered with the solid fats and oils of the high-melting point, the application range is limited, and especially the application to liquefied products becomes very difficult.

[0007]In the latter, the W/O emulsifying composition whose internal aqueous phase is about 0.2-5 micrometers is obtained, Since the L-ascorbic acid of what spreading is in a solution state, the physical intensity of an application range of an emulsification interface is weak, Since it is the fluid / fluid interface of a W/O emulsification type [ becoming easy to produce decomposition etc. and ] when it passes through heating processes, such as sterilization, when it is exposed to physical stress, such as stirring and pumping, there is a fault in which an emulsified state tends to carry out phase inversion destruction.

[0008]

[Problem(s) to be Solved by the Invention]The purpose of this invention is to provide the collagen synthesis accelerator which has the collagen synthesis facilitatory effect which was extremely excellent in stability by maintaining L-ascorbic acid and its derivative at stability for a long period of time.

[0009]

[Means for Solving the Problem]A result of having inquired wholeheartedly in order that this invention persons might solve the aforementioned technical problem, A collagen synthesis accelerator containing L-ascorbic acid, a nonionic surface active agent, and neutral lipid, It finds out having the collagen synthesis facilitatory effect which was extremely excellent in stability, and having the wrinkles improvement effect excellent in a skin cosmetic which blended this invention collagen synthesis accelerator, and came to complete this invention.

That is, this invention relates to a collagen synthesis accelerator which four or less nonionic surface active agent and the melting point made scatter [ HLB ] the ultrafine-particle-ized L-ascorbic acid with a mean particle diameter of 3 micrometers or less by W/O into neutral lipid 45 ** or less by physical crushing, and a skin cosmetic containing this. This invention persons are checking the L-ascorbic acid sustained-release of the constituent concerned by operation of epidermis moisture by using L-ascorbic acid as the constituent concerned which carried out W/O distribution.

[0010]

[Embodiment of the Invention]L-ascorbic acid in this invention, and its derivative, Especially if it has a collagen synthesis facilitatory effect, do not limit, but. It is the known whitening agent preferably used from the former, and it is insoluble to neutral lipid, and a thing with a character of 3 micrometers or less which can be ultrafine-particle-ized has the good mean particle diameter according to laser diffraction type particle-size-distribution measurement by physical crushing. Although the example of L-ascorbic acid is shown below, it does not limit to these. As an example of L-ascorbic acid, L-ascorbic acid, L-**********- 2-phosphoric ester, L-ascorbic acid-3-phosphoric ester, L-ascorbic acid Di Linh acid ester, L-ascorbic acid Tori phosphoric ester, L-ascorbic acid-2-sulfate ester, L-ascorbic acid-3-sulfate ester, L-**********- 2 sulfonic ester and those sodium salt, potassium salt, magnesium salt, calcium salt, an aluminum salt, barium salt, ammonium salt, ethanolamine salt, a diethanolamine salt, A triethanolamine salt, a monoisopropanolamine salt, a diisopropanolamine salt, a tri-isopropanolamine salt, tricyclohexyl ammonium salt, etc., 2-O-alpha-D-glucopyranosyl L-ascorbic acid, 5-O-alpha-D-glucopyranosyl L-ascorbic acid, 6-O-alpha-D-glucopyranosyl L-ascorbic acid, and 2-O-beta-D-galactopyranosyl L-**********,2,3-di-O-. L-ascorbic acid sugar derivatives, such as (beta-D-glucopyranosyl)-L-ascorbic acid, an ascorbic acid Lynn amide derivative, Ascorbic acid-hydroxycarboxylic acid combination, ascorbic acid-arbutin combination, etc. are mentioned. Although use of frost shattering using dry type crushers, such as wet mills, such as KOBORUMIRU, and a jet mill, or liquid nitrogen, etc. is mentioned about a physical crushing method, It does not interfere, even if it will use any, if it is a thing of the performance which can perform 1 micrometer or less of ultrafine particle-ization of 0.5 micrometer or less still more preferably preferably [ mean particle diameter of 3 micrometers or less ] by laser diffraction type particle-size-distribution measurement. If mean particle diameter becomes larger than 3 micrometers, the dispersion stability in the inside of neutral lipid will fall, and the particles of L-ascorbic acid will carry out precipitation separation.

[0011]Although the content in particular of the L-ascorbic acid of this invention does not limit, it is 15 to 50 % of the weight that it is 1 to 70 % of the weight among this constituent desirable still more preferably. When there is less quantity of L-ascorbic acid than 1 % of the weight, the quantity of the L-ascorbic acid which is base resin becomes a very small quantity, and

business as a collagen synthesis accelerator is not accomplished. When there is more quantity of L-ascorbic acid than 70 % of the weight, since structural viscosity increases in a degree very much and loses mobility, a next working characteristic and application range will be narrowed remarkably.

[0012]Although the nonionic surface active agent in particular used for this invention is not limited, The glycerine fatty acid ester which can be preferably offered as skin external preparations, Propylene glycol fatty acid ester, a sorbitan fatty acid ester, Glycerin alkyl ether, polyoxyethylene (it abbreviates to POE- below) fatty acid ester, A POE-glycerine fatty acid ester, a POE-sorbitan fatty acid ester, POE-sorbitol fatty acid ester, POE-alkyl ether, POE-glycerin alkyl ether, POE-alkylphenyl ether, POE-polyoxypropylene glycol, POE-polyoxypropylene alkyl ether, POE-castor oil, POE-hydrogenated castor oil, polyethylene glycol fatty acid ester, etc. are at best still more preferred, and a four or less HLB nonionic surface active agent is good. Although the example of a nonionic surface active agent is shown below, it does not these-limit. As an example of a nonionic surface active agent, glycerin mono- fatty acid ester, glycerin difatty ester, organic acid monoglyceride, polyglyceryl fatty acid ester, and polyglycerin condensation ricinoleic acid ester, Preferably Glycerol monostearate, glycerin mono- olate, a glycerin mono- millimeter state, a glycerin mono-KAPURI rate, glycerin distearate, glycerin diolate, citrate glyceride, malic acid glyceride, acetic acid glyceride, succinic acid glyceride, Lactic acid glyceride, diacetyltartaric acid glyceride, One sort chosen from acetylamino acid glyceride, glyceride pyroglutamate, polyglycerin of the average degrees of polymerization 2-10, fatty acid ester of the carbon numbers 6-22, and polyglycerin of the average degrees of polymerization 2-10 and ester of the poly ricinoleic acid of the degrees 2-4 of condensation. Or propylene glycol fatty acid ester, such as glycerine fatty acid esters, such as two or more sorts of mixtures, propylene glycol monostearate, and propylene glycol mono- olate. Sorbitan fatty acid ester species, such as sorbitan distearate, sorbitan tristearate, sorbitansesquiolate, sorbitan diolate, and a sorbitan trio rate, Glycerin alkyl ether, such as mono- isostearyl glyceryl ether and mono- millimeter still glyceryl ether, is mentioned. Although a nonionic surface active agent is blended one to 100% of the weight to neutral lipid, It is impossible to fully distribute an L-ascorbic acid particle crystal, when an addition is less than 1 % of the weight, When more than 100 % of the weight and making a drainage system distribute this constituent anew, it becomes easy to produce the elution of L-ascorbic acid particles included according to emulsification phase inversion, and interferes with constituting a stable W/O/W emulsification system.

[0013]Although the neutral lipid in particular used for this invention does not limit, fatty acid ester, Synthetic oil fat and soybean oil, such as polyhydric alcohol fatty acid ester, medium-chain-fatty-acid triglyceride, and those hydrogenation things, Rice bran oil, oleum rapae, cottonseed cake oil, sesame oil, safflower oil, castor oil, olive oil, Either of animal fat and oil,

such as vegetable oil and fat, such as cacao seed oil, camellia oil, sunflower oil, palm oil, a flax oil, a beefsteak plant oil, the Xia oil, an ape oil, palm oil, haze wax, jojoba oil, grape seed oil, an avocado oil, and a meadowfoam, a mink oil, yolk oil, beef tallow, milk fat, and lard, can be used. The neutral lipid used for this invention is not included and hindered by hydrocarbon, such as squalane, squalene, a liquid paraffin, an impala fin, and silicone oil, and straight mineral oil, either. furthermore -- although it does not interfere at all even if phospholipid, the sterol, waxes, and oil-soluble vitamins etc. which are originally contained in these live together -- the melting point -- warming at 45 ** or less -- the oil component which can be used in a region is desirable still more preferred, and the melting point is below ordinary temperature. Since two or more heating processes are needed at the time of the addition to preparation, cosmetics, etc. of a collagen synthesis accelerator when the neutral lipid whose melting point is higher than 45 ** is used, a strong heat history will be given to L-ascorbic acid, and an application range will also be narrowed.

[0014]The collagen synthesis accelerator etc. which are prepared by the skin cosmetic of this invention like ****. The surface-active agent used for general cosmetics, oil and fat, polyhydric alcohol, lower alcohol, a thickener, an ultraviolet ray absorbent and a dispersion agent, an antiseptic, an antioxidant, a chelating agent, a pH adjuster, perfume, coloring matter, water, etc. can be blended suitably. It is as follows when the example of these addition ingredients is shown. As a surface-active agent, polyoxyethylene (it abbreviates to POE- below) octyldodecyl alcohol, POE-branching alkyl ether, such as POE-2-decyl tetradecyl alcohol, POE-alkyl ether, such as POE-oleyl alcohol ether and POE-cetyl alcohol ether, Sorbitan ester, such as sorbitan monooleate, sorbitan monoisostearate, and sorbitan monolaurate, POE-sorbitan monooleate, POE-sorbitan monoisostearate, POE-sorbitan ester, such as POE-sorbitan monolaurate, Glycerine fatty acid esters, such as glycerin monooleate, glycerol monostearate, and a glycerin mono- millimeter state, POE-glycerin monooleate, POE-glycerol monostearate, POE-glycerine fatty acid esters, such as a POE-glycerin mono- millimeter state, POE-alkyl aryl ether, such as POE-hydrogenated-castor-oil fatty acid ester, such as a POE-dihydrocholesterol ester, POE-hydrogenated castor oil, and POE-hydrogenated-castor-oil isostearate, and POE-octylphenyl ether, mono- isostearyl glyceryl ether. Glycerin alkyl ether, such as mono- millimeter still glyceryl ether, POE-glycerin alkyl ether, such as POE-monostearyl glyceryl ether and POE-MONOMIRI glyceryl still ether, Diglyceryl monostearate, decaglyceryl deca stearate, Nonionic surface active agents, such as polyglyceryl fatty acid ester, such as decaglyceryl deca isostearate and diglyceryl diisostearate, Myristic acid, stearic acid, pulmitic acid, behenic acid, isostearic acid, The potassium of higher fatty acid, such as oleic acid, sodium, diethanolamine, Salts, such as triethanolamine and amino acid, the above-mentioned alkali salt of ether carboxylic acid, Anionic surfactants, such as a salt of N-acylamino acid, N-acyl SARUKON acid chloride, and a high-class alkyl-sulfonic-acid salt, Ampholytic surface active agents, such

as cationic surfactants, such as an alkylamine salt, polyamine, amino alcohol fatty acid organicity silicone resin, and alkyl quarternary ammonium salt, or lecithin, and a betaine derivative etc.

[0015]As oil and fat, castor oil, olive oil, cacao seed oil, camellia oil, palm oil, Vegetable oil and fat, such as haze wax, jojoba oil, grape seed oil, and an avocado oil. Animal fat and oil, such as a mink oil and yolk oil, yellow bees wax, spermaceti wax, lanolin, a carnauba wax, Lows, such as a candelilla low, a liquid paraffin, squalene, microcrystallin wax, Hydrocarbon, such as a ceresin wax, paraffin wax, and vaseline. Lauric acid, myristic acid, stearic acid, oleic acid, isostearic acid, Nature, such as behenic acid, and synthetic fatty acid, cetanol, stearyl alcohol, Ester species, such as nature, such as hexyldecanol, octyldecanol, and lauryl alcohol, and higher alcohol, myristic acid isopropyl, pulmitic acid isopropyl, myristic acid octyldodecyl, oleic acid octyldodecyl, and cholesterol orate. As polyhydric alcohol, ethylene glycol, a polyethylene glycol, Propylene glycol, a 1,3-butylene glycol, a 1,4-butylene glycol, Polyglycerin, such as dipropylene glycol, glycerin, diglycerol, triglycerol, and tetraglycerin, glucose, malt sugar, multi-TOSU, sucrose, fructose, xylitose, sorbitol, a maltotriose, a sleigh toll, erythritol, etc. As a thickener, sodium alginate, xanthan gum, aluminum silicate, Naturally-ocurring-polymers substances, such as quince seed extracts, tragacanth gum, starch, collagen, and hyaluronate sodium, Synthetic macromolecule substances, such as semisynthesis polymeric materials, such as methyl cellulose, hydroxyethyl cellulose, carboxymethyl cellulose, soluble starch, and cation-ized cellulose, a carboxyvinyl polymer, and polyvinyl alcohol etc.

[0016]As an ultraviolet ray absorbent, p aminobenzoic acid, Para methoxycinnamic acid isopropyl, Butyl methoxy benzoylmethane, glyceryl mono-2-ethylhexanoyl **-**** methoxybenzophenone, JIGAROIRUTORIOREETO, 2-2'-**********- 4-methoxybenzophenone, Ethyl-4-screw hydroxypropyl amino benzoate, 2-ethylhexyl 2-cyano 3,3'-diphenyl acrylate, Para methoxycinnamic acid ethylhexyl, salicylic acid-2-ethylhexyl, Glyceryl para-aminobenzoate and salicylic acid gay methyl, alt.aminobenzoic acid methyl, 2-hydroxy-4-methoxybenzophenone, amyl ****- dimethylamino benzoate, 2-phenylbenzo imidazole 5-sulfonic acid, 2-hydroxy-4-methoxybenzophenone 5-sulfonic acid, etc. As an antiseptic, a benzoate, salicylate, sorbic acid salt, a dehydroacetic acid salt, A paraoxybenzoic acid, 2,4,4'-trichloro-2'-hydroxydiphenyl ether, 3,4,4'-trichlorocarbanilide, a benzalkonium chloride, hinokitiol, resorcinol, ethanol, etc. As an antioxidant, they are tocopherol, ascorbic acid, burylhydroxyanisole, dibutylhydroxytoluene, NORUJI hydronalium guaiaretic acid, propyl gallate, etc. As a chelating agent, they are disodium edetate, sodium acid citrate, etc. A thing with the work which raises the validity of the skin cosmetic of this invention more is also in these addition ingredients by improving the stability or percutaneous absorption of an essential ingredient of this invention.

[0017]A collagen synthesis promotion operation of the other known as a substance which

heightens the wrinkles depressor effect of this invention skin cosmetic, collagenase activity inhibitory action, collagen bridge construction / insolubilization depressant action, a decomposition promotion operation of insoluble collagen, Mucopolysaccharide fragmentation depressant action, such as mucopolysaccharide composition promotion operations, such as hyaluronic acid, hyaluronidase activity inhibitory action, and hyaluronic acid, The substance which has an elastin composition promotion operation, an elastase activity inhibition operation, Maillard reaction inhibitory action, etc., It is also possible to combine the substance which has the above operations of a collagen metabolism activator, an L-ascorbic acid incorporation accelerator, a cutis fibroblast activator, a growth accelerator, etc. which speed up a rebirth or metabolic turnover of collagen, hyaluronic acid, and elastin directly or indirectly. Namely, the estradiol, testosterone, the transformation growth factor (TGF) which have a collagen synthesis promotion operation - beta, vitamin A, betulic acid, Asia acid, Horse mackerel ACHIKOSHIDO, alpha-hydroxy acid and its salt, a benzoic acid amide compound, a sericin decomposition product, a shell membrane decomposition product, a placenta extract, a milk serum fraction, a Ganoderma extract, the U.S. protein breakdown thing, a rice bran decomposition product, a Eucommia-ulmoides-bark leaf extract, And the substance which has a collagen synthesis promotion operation of other known, the Rosmer phosphoric acid which has collagen bridge construction depressant action, the Lamiaceae plant extract, the Ampelopsis japonica extract, vitamin $B_6$, and its derivative, And the substance which has other known collagen bridge construction / insolubilization depressant action, The silk hydrolyzate which has a decomposition promotion operation of insoluble collagen, its ester derivative, and the substance which has a decomposition promotion operation of other known collagen, Various plant extracts, such as collagenase inhibitor, an animal cartilage extract, the Artemisia plant extract, etc. which have a collagenase inhibiting activity operation, and the substance which has a collagenase activity inhibition operation of other known, Mucopolysaccharide composition promotion operations, such as hyaluronic acid. The isoflavonoid series compound called plant estrogen, such as genistein, die zein, a MIROE stole, etc. which it has, a lavender extract, a yeast extract, insulin-like growth factor-1, an epidermal growth factor, interleukin 1, phorbol ester, And the substance which has mucopolysaccharide composition promotion operations, such as other known hyaluronic acid, The chondroitin sulfate which has hyaluronidase activity inhibitory action and its salt, a cardanol derivative, and the substance that has other known hyaluronidase activity inhibitory action, Mucopolysaccharide fragmentation depressant action, such as hyaluronic acid, or decomposition inhibitory action. Crude drug extracts, such as the vitamin E which it has, glutathione, glutathione peroxidase, sault peroxy Dodis mutase, a quercetin derivative, uric acid, transferrin, ceruloplasmin, astaxanthin, cinnamon, GOKAHI, Houttuynia, and caryophylli flos, And the substance which has other known mucopolysaccharide fragmentation depressant

action, such as hyaluronic acid, or decomposition inhibitory action, the erythorbic acid which has an elastin composition promotion operation and its derivative, a green tea extract, and the substance that has an elastin composition promotion operation of other known, A cutis fibroblast activation operation. Nucleic acid related compounds, such as alpha-hydroxy acid, such as adenyl derivatives, such as adenosine triphosphate which it has, and adenosine monophosphate, and those salts, glycolic acid, lactic acid, and salicylic acid, and those derivatives, and ribonucleic acid, an epidermal growth factor, a fibroblast growth factor, And it is possible to combine the substance etc. which have a cutis fibroblast activation operation of other known, and, thereby, the synergistic effect of wrinkles formation control and wrinkles reduction can also be given. The pharmaceutical form of this invention skin cosmetic may also be arbitrary, and also any may be sufficient as soluble, an emulsification system, a powder dispersed system, etc., and, of course, a use can also use broadly basic cosmetics, such as face toilet, a milky lotion, cream, and a pack, charges of face make up, such as foundation, an eyeliner, the cosmetics for bathing, etc.

[0018]Although an example and the example of an examination explain the collagen synthesis accelerator and skin cosmetic of this invention below, it is not restricted to the contents.

[0019]

[Example]Medium-chain-fatty-acid triglyceride 50 weight section whose carbon numbers of example 1 constituent fatty acids are 8 and 10 ($C_8$:$C_{10}$=3:1) (melting point-11 **, TAIYO KAGAKU CO., LTD. make), Polyglycerin condensation ricinoleic acid ester 10 weight section (SunSoft 818H;HLB1, TAIYO KAGAKU CO., LTD. make) is mixed, The oily suspension which added L-ascorbic acid crystal 40 weight section (mean particle diameter of about 100 micrometers, Nippon Roche, Inc. make) is prepared, This was hung on KOBORUMIRU (made by Shinko Pantec Co., Ltd.), and the collagen synthesis accelerator which is the W/O dispersed composition from which the mean particle diameter of L-ascorbic acid was set to 0.4 micrometer by laser diffraction type particle-size-distribution measurement was obtained.

[0020]Example 2 rapeseed refined oil 70 weight section (melting point of 12 **), Polyglycerin condensation ricinoleic acid ester 5 weight section (SunSoft 818H;HLB1, TAIYO KAGAKU CO., LTD. make) and polyglycerin stearic-acid-ester 5 weight section (SANFATTO PS-68;HLB3.5, TAIYO KAGAKU CO., LTD. make) are mixed, L-ascorbic acid mono- magnesium phosphate salt crystal 20 weight section (the mean particle diameter of about 100 micrometers) Prepare the oily suspension which added the Takeda Chemical Industries, Ltd. make, and this is hung on KOBORUMIRU (made by Shinko Pantec Co., Ltd.), The collagen synthesis accelerator which is the W/O dispersed composition from which the mean particle diameter of the L-ascorbic acid mono- magnesium phosphate salt crystal was set to 0.35 micrometer by laser diffraction type particle-size-distribution measurement was obtained.

[0021]Medium-chain-fatty-acid triglyceride 50 weight section whose carbon numbers of

example 3 constituent fatty acids are 8 and 10 ($C_8$:$C_{10}$=3:1) (melting point-11 **, TAIYO KAGAKU CO., LTD. make), Polyglycerin condensation ricinoleic acid ester 5 weight section (SunSoft 818 SX;HLB 0.5, TAIYO KAGAKU CO., LTD. make), Citrate monoglyceride 5 weight section (SunSoft 623M;HLB4, TAIYO KAGAKU CO., LTD. make) is mixed, The oily suspension which added L-ascorbic acid crystal 40 weight section (mean particle diameter of about 100 micrometers, Nippon Roche, Inc. make) is prepared, This was hung on KOBORUMIRU (made by Shinko Pantec Co., Ltd.), and the collagen synthesis accelerator which is the W/O dispersed composition from which the mean particle diameter of L-ascorbic acid was set to 0.4 micrometer by laser diffraction type particle-size-distribution measurement was obtained.

[0022]Medium-chain-fatty-acid triglyceride 50 weight section whose carbon numbers of the stability test constituent fatty acids of example of examination 1. L-ascorbic acid are 8 and 10 ($C_8$:$C_{10}$=3:1) (melting point-11 **, TAIYO KAGAKU CO., LTD. make), Polyglycerin condensation ricinoleic acid ester 10 weight section (SunSoft 818H;HLB1, TAIYO KAGAKU CO., LTD. make) is mixed, High speed stirring was performed in the homomixer (made by special opportunity-ized industrial incorporated company), adding L-ascorbic acid solution 40 weight section (pH 2.0) 10%, and the W/O emulsified liquid from which the mean particle diameter of the internal aqueous phase was set to 0.4 micrometer by laser diffraction type particle-size-distribution measurement was prepared. The oxidation stability of L-ascorbic acid in the collagen synthesis accelerator which is a W/O dispersed composition of Example 1 was compared by considering this as contrast.

[0023]Confine 200 g of both each in a pressure bottle, respectively, and 121 ** and heat sterilization for 30 minutes are performed, Isolate 20 g preparatively after radiational cooling, add 200 ml of metalline 2% acid aqueous solutions, and 200 ml of n-hexane, and shaking extraction is carried out under a room temperature, The obtained water layer portions were collected, and it filtered with a 0.45-micrometer membrane filter, and was considered as test liquid, and the amount of L-ascorbic acid was measured by HPLC which installed the amide bond type opposite phase column (the amide 80, TOSOH CORP. make). The elution solvent measured detection with the absorbance of 254 nm using acetonitrile / 2.5mM potassium phosphate solution (50/50). Then, both were saved for three months at 50 **, the same measurement as the above was performed for every month, and the emulsified state was observed.

[0024]L-ascorbic acid will be decomposed into oxalic acid etc. through 2,3-diketo gulonic acid, if a hydrogen atom is easily lost from the enal group of the 2nd place and the 3rd place under water existence, and it becomes dehydroascorbic acid which is a keto form isomer and also oxidation progresses. Since there was character in which only L-ascorbic acid in these compounds presents specific absorption to the wavelength which is 254 nm, the survival rate

of L-ascorbic acid was searched for by having made this into the index, and the stability as L-ascorbic acid was compared.

[0025]As a result, as shown in Table 1, in the collagen synthesis accelerator of Example 1, attenuation of L-ascorbic acid hardly arose, but the outstanding stable voltinism was shown.

[0026]

[Table 1]

L－アスコルビン酸の安定性比較

| 項　目 | L－アスコルビン酸残存率（%） | | | | 乳化状態 |
|---|---|---|---|---|---|
| | 殺菌直後 | 1ヶ月保存 | 2ヶ月保存 | 3ヶ月保存 | |
| 実施例1 | 99．5 | 97．2 | 95．0 | 95．0 | 安定 |
| 試験例1（対照） | 70．5 | 61．3 | 52．2 | 48．1 | 2週間で分離 |

[0027]The stability test of example of examination 2. L-ascorbic acid (at the time of W/O/W emulsification)

Medium-chain-fatty-acid triglyceride 50 weight section whose carbon numbers of constituent fatty acids are 8 and 10 ($C_8$:$C_{10}$=3:1) (melting point-11 **, TAIYO KAGAKU CO., LTD. make), Polyglycerin condensation ricinoleic acid ester 10 weight section (SunSoft 818H;HLB1, TAIYO KAGAKU CO., LTD. make) is mixed, High speed stirring was performed in the homomixer (made by special opportunity-ized industrial incorporated company), adding L-ascorbic acid solution 40 weight section (pH 2.0) 10%, and the W/O emulsified liquid from which the mean particle diameter of the internal aqueous phase was set to 0.4 micrometer by laser diffraction type particle-size-distribution measurement was prepared. This was added into the water 1000 weight section in which sucrose-fatty-acid-ester 5 weight section (the Ryoto sugar ester S-1670, the Mitsubishi Chemical, Inc. make) was dissolved, was stirred, and W/O/W emulsified liquid was prepared.

[0028]Similarly, also add the W/O dispersed composition of Example 3 into the water 1000 weight section in which sucrose-fatty-acid-ester 5 weight section (the Ryoto sugar ester S-1670, the Mitsubishi Chemical, Inc. make) was dissolved, stir it, and W/O/W emulsified liquid is

prepared, Confine 200 g of both each in a pressure bottle, respectively, and 121 ** and heat sterilization for 15 minutes are performed, Isolate 50 g preparatively after radiational cooling, add 200 ml of metalline 2% acid aqueous solutions, and 200 ml of n-hexane, and shaking extraction is carried out under a room temperature, The obtained water layer portions were collected, and it filtered with a 0.45-micrometer membrane filter, and was considered as test liquid, and the amount of L-ascorbic acid was measured by HPLC which installed the amide bond type opposite phase column (the amide 80, TOSOH CORP. make). The elution solvent measured detection with the absorbance of 254 nm using acetonitrile / 2.5mM pqtassium phosphate solution (50/50). Then, both were saved for three weeks at 40 **, the same measurement as the above was performed weekly, and the emulsified state was observed.
[0029]As a result, the collagen synthesis accelerator which is a W/O dispersed composition of Example 3 as shown in Table 2 showed the stable voltinism which attenuation of L-ascorbic acid hardly arose, but was excellent under the unstable W/O/W type emulsification condition.
[0030]
[Table 2]

Ｌ－アスコルビン酸の安定性比較（Ｗ／Ｏ／Ｗ乳化時）

| 項　目 | Ｌ－アスコルビン酸残存率（％） | | | | 乳化状態 |
|---|---|---|---|---|---|
| | 殺菌直後 | 1週間保存 | 2週間保存 | 3週間保存 | |
| 実施例3 | 97．0 | 95．0 | 94．3 | 94．1 | 安定 |
| 試験例2（対照） | 51．2 | 45．0 | 38．7 | 30．2 | 2週間で分離 |

[0031]The stability test of example of examination 3. L-ascorbic acid (addition to face toilet) Collagen synthesis accelerator 3 weight section of Example 3 was added to face toilet 100 commercial weight section, stirring mixing was carried out, and the L-ascorbic acid content face toilet of 1200 mg/g was prepared. The face toilet which carried out the addition dissolution of the L-ascorbic acid 1.2 weight section as contrast at face toilet 100 same weight section was prepared, and it compared about the survival rate of L-ascorbic acid in both.

[0032]When the L-ascorbic acid survival rate was analyzed based on the measuring method method of the example 2 of an examination, in the contrast article, the survival rate in that in which the survival rate received that it was at 28.7%, and added the collagen synthesis accelerator of Example 3 is 94.5%, and has fully checked the effect of this invention in the cosmetics of a drainage system.

[0033]The collagen synthesis promotion ability examination of an example of examination 4. cultured fibroblast (S. method of B.Russel (Biochemistry, 10, 988, 1971), and B.Peterkofsky and others (J. Cell.Physiol., 97, 221, 1978))

Hexane was added to the collagen synthesis accelerator 1g of Example 1, after repeating washing by hexane to the sediment obtained by centrifugal separation, vacuum drying of the sediment concerned was carried out in the dark place in a refrigerator, and hexane was removed thoroughly. After dissolving the obtained dry matter in 200 ml of water, filtration sterilization was carried out and it was considered as the sample A of the exam. Operation with the same said of what saved 40 ** of collagen synthesis accelerators of Example 1 for six months was carried out, and it was considered as the sample B. To next, the WI-38 cell (Homo sapiens embryo lung normal diploid cell) which has carried out subculture. Under the low blood serum culture condition of a MEM culture medium (0.5% fetal-calf-serum content), after adding the solution of said sample, It cultivated for 37 ** and four days in 5%$CO_2$+95%Air, and

50microl addition of $^3$H-proline (200 microcurie/(ml)) was done into 5 ml of culture media, and 37 ** was cultivated in 5%$CO_2$+95%Air for 6 hours. The sample additive-free division was considered as contrast. Removed the culture supernatant after that, 37 ** collagenase type = (made by Worthington)5units/ml was made to act on a cell fraction for 18 hours, the trichloroacetic acid solution performed deproteinization, the meltable fraction was mixed with the HAIO nick flow, and the dose of radiation was measured. Although the solvent removed neutral lipid and a nonionic surface active agent and the bottom reduced pressure drying of low temperature removed the solvent in consideration of adding a sample directly to a cultured cell in evaluation of collagen synthesis promotion ability, this does not restrict the collagen synthesis accelerator of this invention.

[0034]The following of the addition to the culture medium of said sample is carried out.

Addition (V/V culture medium %)

Sample A : 0.5% Sample B : 0.5%[0035]Although the result was shown in Table 3, on the preservation conditions under 40 ** and the abuse conditions for six months, collagen synthesis promotion activity was not lost after collagen synthesis accelerator preparation. This result of be [ it / what the preservation stability of the L-ascorbic acid included by this invention collagen synthesis accelerator depends on a very good thing over a long period of time ] is clear.

[0036]
[Table 3]

| 試料 | コラーゲン量（dpm／$10^2$ cells）＊ |
|---|---|
| 対照 | 1．89±0．10 |
| A | 5．71±0．24＊＊ |
| B | 5．58±0．13＊＊ |

＊　：細胞当たりのコラーゲン量

＊＊：対照との間に信頼度99％で有意差あり（n＝4）

[0037]The closed patch test was carried out to the 16 men of 21-55 years old of example of examination 5. patch test age, 14 women, and the upper arm flexor of the subject which consists of a total of 30 persons. The collagen synthesis accelerator of Examples 1-3 was used as a sample.
[0038]standard of a judgment - : -- completely -- adiaphorous and **: -- minor erythema and +: -- clear erythema, ++:erythema and swelling, and papule [0039]As a result, there were dramatically few possibilities that it would be - (completely adiaphorous) and each sample would cause a stimulus reaction and an allergic reaction in all the subject, and they were high, and it became clear that it is what can be blended with a skin cosmetic. [ of the safety of the collagen synthesis accelerator of this invention ]
[0040]It is targeted at 50 women aged (40.2 years old of average age) from 30 to 45 who have a trouble of example of examination 6. panel test 1 fine lines, The organic-functions evaluation of the result which made 25 persons of a half apply to the face the cream (contrast skin cosmetic) of the formula excluding the collagen synthesis accelerator of Example 2 from Example 5 in the remaining half in the milky lotion of Example 6 which is the below-mentioned this invention skin cosmetic for bis die (morning, the evening) continuation three months and for which they were made to use it was shown in Table 4.
[0041]
[Table 4]

| 試料 | 評価 | 皺（人） | きめ（人） | しっとり（人） |
|---|---|---|---|---|
| 本発明 | 有効 | 10 | 11 | 9 |
| 皮膚化粧料 | やや有効 | 10 | 13 | 12 |
| | 無効 | 5 | 1 | 4 |
| 対照 | 有効 | 0 | 0 | 0 |
| 皮膚化粧料 | やや有効 | 2 | 5 | 11 |
| | 無効 | 23 | 20 | 14 |

[0042]clearer than Table 4 -- as -- this invention skin cosmetic of Example 6 -- wrinkles and texture -- in admiration, high validity was shown gently. It is clear that this effect's it is what is depended on this invention collagen synthesis accelerator contained in this invention skin cosmetic.

[0043]The panel test was done about this invention skin cosmetic which targeted for the mothball 50 women aged from 28 to 45 who have a trouble of example of examination 7. panel test 2 fine lines. In the remaining half, the contrast skin cosmetic was applied to 25 of 50 women of a half for the below-mentioned this invention skin cosmetic for bis die (morning, the evening) continuation three months at the face. In this invention skin cosmetic, prepare the cream of Example 5, and the collagen synthesis accelerator of Example 1 is removed from Example 5 to a contrast skin cosmetic, The cream which contains the cream of Example 5 and L-ascorbic acid of the concentration by the formula which used L-ascorbic acid solution 40% instead was prepared, and what saved 40 ** of each cosmetics for six months after preparation, respectively was used. The result of organic-functions evaluation is shown in Table 5.

[0044]

[Table 5]

| 試料 | 評価 | 皺（人） | きめ（人） | しっとり（人） |
|---|---|---|---|---|
| 本発明 | 有効 | 8 | 12 | 8 |
| 皮膚化粧料 | やや有効 | 12 | 11 | 14 |
| | 無効 | 5 | 2 | 3 |
| 対照 | 有効 | 0 | 0 | 0 |
| 皮膚化粧料 | やや有効 | 1 | 4 | 5 |
| | 無効 | 24 | 21 | 20 |

[0045]the direction of this invention skin cosmetic which added this invention collagen synthesis accelerator prevents the wrinkles of skin so that more clearly than Table 5 -- texture -- the warm wet thing to do for the skin was accepted. It was checked that it is clear that it is what this effect is included in this invention skin cosmetic, and is depended on a **** this invention collagen synthesis accelerator, and after skin cosmetic preparation has the very good preservation stability of the L-ascorbic acid included over a long period of time.
[0046]
example 4 <face toilet> glycerin Five copies . propylene glycol Four copies Oleyl alcohol . Copy [ 0.1 ] Polyoxyethylene Sorbitan Mono- Laurate Ester 1.5 Copies Polyoxyethylene Lauryl Ether 0.5 Copy Ethanol Ten Copies Collagen Synthesis Accelerator of Example 1 Ten-Copy Perfume, Color, Antiseptic, and Ultraviolet Ray Absorbent Optimum Dose Purified Water 68.9 Copies[0047]
example 5 <cream> stearyl alcohol . Copies [ Seven ] Stearic Acid Two Copies Reduction Lanolin . Copies [ Five ] Squalane Six Copies OctiDodecanol Three Copies Polyoxyethylene Cetyl Ether Two Copies Lipophilic Type Glyceryl Monostearate Five Copies Propylene Glycol Five Copies Collagen Synthesis Accelerator of Example 1 Ten Copies Perfume, Antiseptic, and Antioxidant Optimum Dose Purified Water 55 Copies[0048]
example 6 <milky lotion> stearic acid 0.2 copy . cetanol 1.5 copies Vaseline Three copies Lanolin alcohol . Copies [ Two ] Liquid Paraffin Ten Copies Polyoxyethylene MonoOleate Two Copies Glycerin Three Copies Propylene Glycol Five Copies Triethanolamine One Copy Collagen Synthesis Accelerator of Example 2 15 Copies Perfume, Antiseptic, and Antioxidant Optimum Dose Purified Water 57.3 Copies[0049]
Example 7 <pack> polyvinyl alcohol 15 copies Carboxymethylcellulose sodium Five copies Propylene glycol Three copies Ethanol Ten copies Collagen synthesis accelerator of Example 3 Five copies Perfume, an antiseptic, oxidizer Optimum dose Purified water 62 copies[0050]
[Effect of the Invention]Also in the case where the collagen synthesis accelerator of this

invention is stabilized extremely, and various L-ascorbic acid unstable as it is distributes it in drainage system cosmetics, such as face toilet, It is characterized by constituting a stable W/O/W emulsification system, without eluting the L-ascorbic acid included according to emulsification phase inversion. When it applies to the skin, the stable collagen synthesis facilitatory effect is demonstrated, and since safety is also high, the application on clinical is expected. The skin cosmetic containing these collagen synthesis accelerator makes the collagen synthesis facilitatory effect to which L-ascorbic acid stable with the collagen synthesis accelerator concerned originates in the physiological function for a long period of time maintain. Therefore, this invention is enabled to supply the very stable collagen synthesis accelerator which is not in the former simple, and an industrial meaning is dramatically large.

[Translation done.]